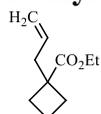


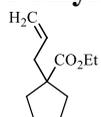
## Synthesis of tetrazole-substituted spirocyclic $\gamma$ -lactams by one-pot azido-Ugi reaction–cyclization

Vasiliy Yu. Stolyarenko, Anatoliy A. Evdokimov and Vladimir I. Shishkin

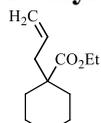
### 1-Allylcyclobutanecarboxylic acid ethyl ester 5

 Yield – 96% (yellowish oil).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 5.71 (m, 1H); 4.98-5.12 (m, 2H); 4.14 (q, 2H,  $J$  7.2 Hz); 2.50 (d, 2H,  $J$  7.6 Hz); 2.36-2.46 (m, 2H); 1.19 (m, 4H); 1.25 (t, 3H,  $J$  7.2 Hz).

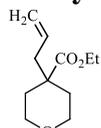
### 1-Allylcyclopentanecarboxylic acid ethyl ester 6

 Yield – 90% (yellowish oil).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 5.71 (m, 1H); 4.96-5.08 (m, 2H); 4.12 (q, 2H,  $J$  7.2 Hz); 2.35 (d, 2H,  $J$  7.4 Hz); 2.02-2.14 (m, 2H); 1.64 (m, 4H); 1.47-1.58 (m, 2H); 1.25 (t, 3H,  $J$  7.2 Hz).

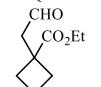
### 1-Allylcyclohexanecarboxylic acid ethyl ester 7

 Yield – 93% (yellow oil).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 5.71 (m, 1H); 4.95-5.07 (m, 2H); 4.15 (q, 2H,  $J$  7.2 Hz); 2.24 (d, 2H,  $J$  7.6 Hz); 1.98-2.15 (m, 2H); 1.50-1.66 (m, 2H); 1.16-1.45 (m, 9H).

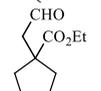
### 4-Allyltetrahydropyran-4-carboxylic acid ethyl ester 8

 Yield – 98% (colourless oil).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 5.70 (m, 1H); 4.98-5.14 (m, 2H); 4.19 (q, 2H,  $J$  7.2 Hz); 3.77-3.89 (m, 2H); 3.40-3.53 (m, 2H); 2.25-2.35 (m, 2H); 2.06-2.13 (m, 2H); 1.49-1.59 (m, 2H); 1.28 (t, 3H,  $J$  7.2 Hz).

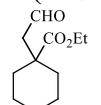
### 1-(2-Oxoethyl)cyclobutanecarboxylic acid ethyl ester 9

 Yield – 93% (colourless oil).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 9.73 (s, 1H); 4.18 (q,  $J$  6.8 Hz, 2H); 2.72 (s, 2H); 2.52-2.68 (m, 2H); 1.91-2.12 (m, 4H); 1.27 (t,  $J$  6.8 Hz, 3H)

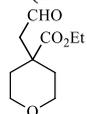
### 1-(2-Oxoethyl)cyclopentanecarboxylic acid ethyl ester 10

 Yield – 93% (yellowish oil).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 9.73 (s, 1H); 4.15 (q,  $J$  7.0 Hz, 2H); 2.72 (s, 2H); 2.13-2.27 (m, 2H); 1.52-1.84 (m, 6H); 1.25 (t,  $J$  7.0 Hz, 3H)

### 1-(2-Oxoethyl)cyclohexanecarboxylic acid ethyl ester 11

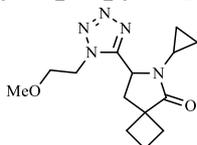
 Yield – 93% (yellow oil).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 9.73 (s, 1H); 4.18 (q,  $J$  7.0 Hz, 2H); 2.63 (s, 2H); 1.93-2.15 (m, 2H); 1.35-1.59 (m, 8H); 1.27 (t,  $J$  7.0 Hz, 3H)

#### 4-(2-Oxoethyl)tetrahydropyran-4-carboxylic acid ethyl ester **12**



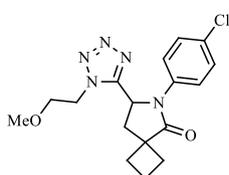
Yield – 93% (yellowish oil).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 9.74 (s, 1H); 4.23 (q,  $J$  7.2 Hz, 2H); 3.74-3.81 (m, 2H); 3.60-3.70 (m, 2H); 2.71 (s, 2H); 2.11-2.20 (m, 2H); 1.58-1.70 (m, 2H); 1.28 (t,  $J$  7.2 Hz, 3H);

#### 6-Cyclopropyl-7-[1-(2-methoxyethyl)-1H-tetrazol-5-yl]-6-azaspiro[3.4]octan-5-one **13a**



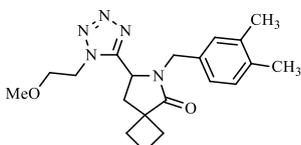
Yield – 52%, white solid, mp 89-90°C.  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 4.95 (dd, 1H,  $J$  8.2, 5.6 Hz); 4.46-4.65 (m, 2H); 3.72-3.90 (m, 2H); 3.32 (m, 3H); 2.47 (m, 1H); 2.31 (dd, 1H,  $J$  12.8, 8.2 Hz); 2.10-2.23 (m, 2H); 1.92-2.03 (m, 1H); 1.76-1.91 (m, 2H); 1.50-1.70 (m, 5H); 0.76-0.86 (m, 1H); 0.61-0.72 (m, 1H); 0.47-0.59 (m, 2H). MS (ESI,  $m/z$ ): 292  $[\text{M}+\text{H}]^+$ , 583  $[2\text{M}+\text{H}]^+$ .

#### 6-(4-Chlorophenyl)-7-[1-(2-methoxyethyl)-1H-tetrazol-5-yl]-6-azaspiro[3.4]octan-5-one **13b**



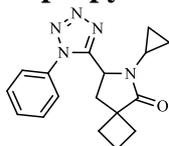
Yield – 55%, gray solid, mp 127-128°C.  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 7.31 (d, 1H,  $J$  8.8 Hz); 7.25 (d, 1H,  $J$  8.8 Hz); 5.64 (dd, 1H,  $J$  8.0, 6.4 Hz); 4.38-4.47 (m, 1H); 4.28-4.37 (m, 1H); 3.76-3.83 (m, 1H); 3.67-3.75 (m, (s, 3H); 2.55 (dd, 1H,  $J$  13.2, 8.0 Hz); 2.02-2.13 (m, 1H); 1.84-1.97 (m, 2H); 1.63-1.79 (m, 4H). MS (ESI,  $m/z$ ): 363  $[\text{M}+\text{H}]^+$ , 725  $[2\text{M}+\text{H}]^+$ .

#### 6-(3,4-Dimethylbenzyl)-7-[1-(2-methoxyethyl)-1H-tetrazol-5-yl]-6-azaspiro[3.4]octan-5-one **13c**



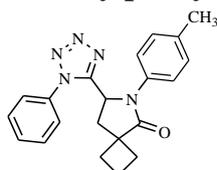
Yield – 59%, yellowish solid, mp 97-98°C.  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 7.04 (d, 1H,  $J$  7.6 Hz); 6.61-6.74 (m, 2H); 5.08 (d, 1H,  $J$  14.8 Hz); 4.68 (t, 1H,  $J$  7.2 Hz); 4.19-4.28 (m, 1H); 3.58-3.70 (m, 2H); 3.55 (d, 1H,  $J$  14.8 Hz); 3.18 (s, 3H); 2.28 (dd, 1H,  $J$  12.8, 7.6 Hz); 2.24 (s, 3H); 2.20 (s, 3H); 2.14 (dd, 1H,  $J$  12.4, 6.8 Hz); 1.96-2.07 (m, 1H); 1.82-1.95 (m, 2H); 1.57-1.75 (m, 5H). MS (ESI,  $m/z$ ): 370  $[\text{M}+\text{H}]^+$ , 541  $[2\text{M}+\text{H}]^+$ .

#### 6-Cyclopropyl-7-(1-phenyl-1H-tetrazol-5-yl)-6-azaspiro[3.4]octan-5-one **13d**



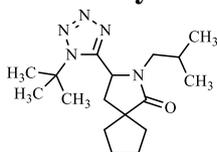
Yield – 67%, beige solid, mp 132-133°C.  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 7.61-7.70 (m, 3H); 7.41-7.49 (m, 2H); 4.79 (dd, 1H,  $J$  8.4, 5.6 Hz); 2.41 (m, 1H); 2.28 (dd, 1H,  $J$  12.8, 8.2 Hz); 2.09-2.21 (m, 2H); 1.88-1.98 (m, 1H); 1.76-1.88 (m, 2H); 1.53-1.67 (m, 3H); 1.42-1.51 (m, 1H); 0.75-0.86 (m, 1H); 0.59-0.69 (m, 1H); 0.42-0.51 (m, 1H); 0.33-0.42 (m, 1H). MS (ESI,  $m/z$ ): 310  $[\text{M}+\text{H}]^+$ , 619  $[2\text{M}+\text{H}]^+$ .

#### 6-(4-Methylphenyl)-7-(1-phenyl-1H-tetrazol-5-yl)-6-azaspiro[3.4]octan-5-one **13e**



Yield – 65%, beige solid, mp 136-137°C.  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 7.56 (t, 1H,  $J$  7.2 Hz); 7.50 (t, 2H,  $J$  7.2 Hz); 7.07 (d, 2H,  $J$  8.0 Hz); 6.99 (d, 2H,  $J$  8.0 Hz); 6.93 (d, 2H,  $J$  8.0 Hz); 5.33 (dd, 1H,  $J$  8.0, 5.2 Hz); 2.73 (dd, 1H,  $J$  13.2, 8.8 Hz); 2.69-2.59 (m, 1H); 2.23 (s, 3H); 2.13-1.89 (m, 4H). MS (ESI,  $m/z$ ): 360  $[\text{M}+\text{H}]^+$ , 719  $[2\text{M}+\text{H}]^+$ .

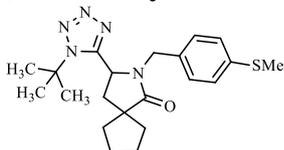
### 3-(1-tert-Butyl-1H-tetrazol-5-yl)-2-isobutyl-2-azaspiro[4.4]nonan-1-one 14a



Yield – 56%, yellowish solid, mp 142-143°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 5.04 (dd, 1H, *J* 8.4, 2.8 Hz); 3.50 (dd, 1H, *J* 14.2, 9.2 Hz); 2.51-2.65 (m, 3H); 2.45 (dd, 1H, *J* 14.2, 6.0 Hz); 2.17 (dd, 1H, *J* 13.2, 3.2 Hz); 2.01-2.12(m, 1H); 1.76-1.95 (m, 4H); 1.73 (s, 9H); 1.53-1.67 (m, 1H);

0.81 (dd, 6H, *J* 6.4, 5.2 Hz). MS (ESI, *m/z*): 320 [M+H]<sup>+</sup>, 639 [2M+H]<sup>+</sup>.

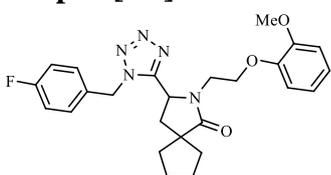
### 3-(1-tert-Butyl-1H-tetrazol-5-yl)-2-(4-methylsulfanylbenzyl)-2-azaspiro[4.4]nonan-1-one 14b



Yield – 72%, beige solid, mp 148-149°C. <sup>1</sup>H-NMR 7.14 (d, 2H, *J* 8.0 Hz); 6.86 (d, 2H, *J* 8.0 Hz); 5.72 (d, 1H, *J* 15.2 Hz); 4.74 (dd, 1H, *J* 8.4, 4.0 Hz); 3.60 (d, 1H, *J* 15.2 Hz); 2.55-2.70 (m, 2H); 2.50 (dd, 1H, *J* 12.8, 8.0 Hz); 2.40 (s, 3H); 2.04-2.19 (m, 2H); 1.87-1.98 (m, 2H);

1.76-1.87 (m, 1H); 1.44 (s, 9H). MS (ESI, *m/z*): 400 [M+H]<sup>+</sup>, 799 [2M+H]<sup>+</sup>.

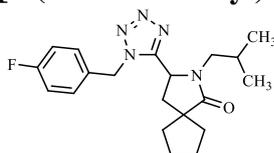
### 3-[1-(4-Fluorobenzyl)-1H-tetrazol-5-yl]-2-[2-(2-methoxyphenoxy)-ethyl]-2-azaspiro[4.4]nonan-1-one 14c



Yield – 56%, yellowish solid, mp 127-128°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 7.17 (dd, 2H, *J* 8.4, 5.6 Hz); 6.92-7.04 (m, 3H); 6.84-6.91 (m, 2H); 6.78 (d, 1H, *J* 7.6 Hz); 5.67 (d, 1H, *J* 15.6 Hz); 5.48 (d, 1H, *J* 15.6 Hz); 5.37 (dd, 1H, *J* 8.0, 4.8 Hz); 4.06-4.13 (m, 1H); 3.92-4.05 (m, 2H); 3.74 (s, 3H); 2.89-3.99 (m, 1H); 2.49-2.61 (m, 1H); 2.37-2.48

(m, 1H); 2.14 (dd, 2H, *J* 12.4, 8.0 Hz); 1.96-2.09 (m, 1H); 1.75-1.94 (m, 4H). MS (ESI, *m/z*): 466 [M+H]<sup>+</sup>, 931 [2M+H]<sup>+</sup>.

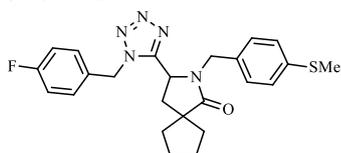
### 3-[1-(4-Fluorobenzyl)-1H-tetrazol-5-yl]-2-isobutyl-2-azaspiro[4.4]nonan-1-one 14d



Yield – 51%, white solid, mp 122-123°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 7.11-7.23 (m, 2H); 7.05 (t, 2H, *J* 8.4 Hz); 5.55 (d, 1H, *J* 15.6 Hz); 5.36 (d, 1H, *J* 15.6 Hz); 4.85 (t, 1H, *J* 6.8 Hz); 3.39 (dd, 2H, *J* 13.6, 9.2 Hz); 2.47-2.62 (m, 1H); 2.31-2.47 (m, 2H); 2.12 (dd, 2H, *J*

13.6, 4.8 Hz); 1.96-2.11 (m, 1H); 1.74-1.94 (m, 3H); 1.60-1.74 (m, 1H); 1.32-1.49 (m, 1H); 0.67 (t, 3H, *J* 5.6 Hz). MS (ESI, *m/z*): 372 [M+H]<sup>+</sup>, 743 [2M+H]<sup>+</sup>.

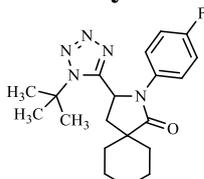
### 3-[1-(4-Fluorobenzyl)-1H-tetrazol-5-yl]-2-(4-methylsulfanylbenzyl)-2-azaspiro[4.4]nonan-1-one 14e



Yield – 65%, beige solid, mp 136-137°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 7.08 (d, 2H, *J* 8.0 Hz); 6.92-7.03 (m, 4H); 6.77 (d, 2H, *J* 8.0 Hz); 5.26 (d, 1H, *J* 15.2 Hz); 4.95 (dd, 1H, *J* 17.6, 15.2 Hz); 4.46 (dd, 1H, *J* 7.6, 6.0 Hz); 3.54 (d, 1H, *J* 15.2 Hz); 2.52-2.63 (m, 1H); 2.37-

2.48 (m + s, 4H); 2.18(dd, 1H, *J* 13.2, 8.0 Hz); 2.01-2.13 (m, 1H); 1.70-1.92 (m, 4H). MS (ESI, *m/z*): 452 [M+H]<sup>+</sup>, 903 [2M+H]<sup>+</sup>.

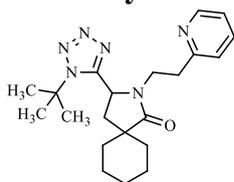
### 3-(1-tert-Butyl-1H-tetrazol-5-yl)-2-(4-fluorophenyl)-2-azaspiro[4.5]decan-1-one 15a



Yield – 52%, yellowish solid, mp >200°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 7.20 (dd, 2H, *J* 8.8, 4.8 Hz); 6.98 (t, 2H, *J* 8.8 Hz); 5.60 (dd, 1H, *J* 8.8, 4.8 Hz); 2.61 (dd, 1H, *J* 12.8, 8.8 Hz); 2.22 (dd, 1H, *J* 12.8, 4.8 Hz); 1.90-2.00 (m, 2H); 1.73-1.90 (m, 4H); 1.66 (s, 9H); 1.53-1.64 (m, 2H); 1.31-1.45 (m, 2H); 1.17-1.31 (m, 1H). MS (ESI, *m/z*): 372

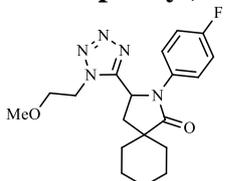
[M+H]<sup>+</sup>, 743 [2M+H]<sup>+</sup>.

### 3-(1-tert-Butyl-1H-tetrazol-5-yl)-2-[2-(pyridin-2-yl)-ethyl]-2-azaspiro[4.5]decan-1-one 15b



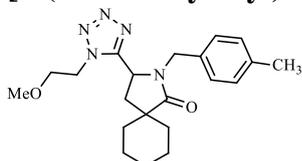
Yield – 58%, yellow solid, mp 137-138°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 8.44 (d, 1H, *J* 4.0 Hz); 7.63 (t, 1H, *J* 6.8 Hz); 7.23 (d, 1H, *J* 7.2 Hz); 7.15 (d, 1H, *J* 5.6 Hz); 5.5 (br. s, 1H); 4.08-4.16 (m, 1H); 3.06-3.15 (m, 2H); 2.60-2.78 (m, 1H); 2.27 (dd, 1H, *J* 13.2, 9.6 Hz); 1.83 (dd, 1H, *J* 12.8, 4.8 Hz); 1.78 (s, 9H); 1.78 (s, 9H); 1.51-1.52 (m, 8H); 1.06-1.32 (m, 4H). MS (ESI, *m/z*): 384 [M+H]<sup>+</sup>, 767 [2M+H]<sup>+</sup>.

### 2-(4-Fluorophenyl)-3-[1-(2-methoxyethyl)-1H-tetrazol-5-yl]-2-azaspiro[4.5]decan-1-one 15c



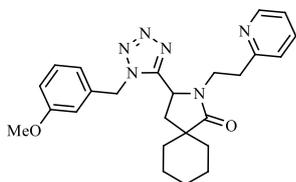
Yield – 50%, white solid, mp 122-123°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 7.22-7.27 (m, 2H); 6.97 (t, 1H, *J* 8.8 Hz); 5.59 (dd, 1H, *J* 8.4, 6.8 Hz); 4.37-4.46 (m, 1H); 4.20-4.30 (m, 1H); 3.72-3.79 (m, 1H); 3.64-3.71 (m, 1H); 3.28 (s, 3H); 2.63 (dd, 1H, *J* 13.2, 8.4 Hz); 3.29 (dd, 1H, *J* 12.8, 6.4 Hz); 1.89-1.99 (m, 1H); 1.73-1.87 (m, 4H); 1.57-1.72 (m, 2H); 1.34-1.46 (m, 2H); 1.24-1.33 (m, 1H). MS (ESI, *m/z*): 374 [M+H]<sup>+</sup>, 747 [2M+H]<sup>+</sup>.

### 3-[1-(2-Methoxyethyl)-1H-tetrazol-5-yl]-2-(4-methylbenzyl)-2-azaspiro[4.5]decan-1-one 15d



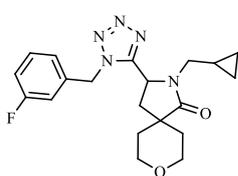
Yield – 58%, beige solid, mp 76-77°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 6.94 (d, 2H, *J* 7.6 Hz); 6.71 (d, 2H, *J* 7.6 Hz); 5.15 (d, 2H, *J* 14.8 Hz); 4.71 (dd, 1H, *J* 8.6, 5.2 Hz); 3.52 (d, 2H, *J* 14.8 Hz); 2.29 (dd, 1H, *J* 12.8, 8.6 Hz); 2.18 (s, 3H); 1.65-1.75 (m, 4H); 1.50-1.65 (m, 4H); 1.35-1.45 (m, 1H); 1.33 (s, 9H); 1.06-1.27 (m, 4H). MS (ESI, *m/z*): 384 [M+H]<sup>+</sup>, 767 [2M+H]<sup>+</sup>.

### 3-[1-(3-Methoxybenzyl)-1H-tetrazol-5-yl]-2-[2-(pyridin-2-yl)-ethyl]-2-azaspiro[4.5]decan-1-one 15e



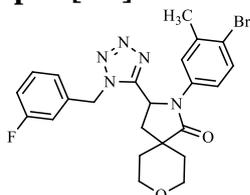
Yield – 50%. beige solid, mp 78-79°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 7.19-7.35 (m, 3H); 6.83-5.98 (m, 2H); 6.51-6.65 (m, 3H); 5.54 (d, 2H, *J* 15.2 Hz); 5.22 (d, 2H, *J* 15.6 Hz); 4.86 (d, 2H, *J* 15.2 Hz); 4.61 (t, 1H, *J* 7.6 Hz); 3.89 (d, 2H, *J* 15.6 Hz); 3.77 (s, 3H); 1.78-1.93 (m, 2H); 1.53-1.75 (m, 5H); 1.41-1.52 (m, 1H); 1.25-1.35 (m, 2H); 0.94-1.17 (m, 2H). MS (ESI, *m/z*): 448 [M+H]<sup>+</sup>, 895 [2M+H]<sup>+</sup>.

### 2-Cyclopropylmethyl-3-[1-(3-fluorobenzyl)-1H-tetrazol-5-yl]-8-oxa-2-azaspiro[4.5]decan-1-one 16a



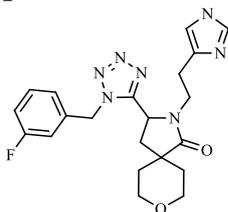
Yield – 55%. White solid, mp 187°C (dec). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 7.25 (dd, 1H, *J* 8.8, 5.2 Hz); 7.13 (t, 1H, *J* 8.0 Hz); 5.56 (s, 2H); 5.18 (dd, 1H, *J* 8.0, 6.4 Hz); 3.91-4.05 (m, 2H); 3.68 (dd, 1H, *J* 14.8, 6.8 Hz); 3.41-5.50 (m, 1H); 3.27-3.36 (m, 1H); 2.38 (dd, 1H, *J* 14.8, 6.8 Hz); 2.28 (dd, 1H, *J* 13.2, 8.4 Hz); 2.06-2.17 (m, 1H); 1.93-2.04 (m, 1H); 1.68 (dd, 1H, *J* 12.8, 6.4 Hz); 1.31-1.42 (m, 2H); 0.50-0.64 (m, 1H); 0.28-0.41 (m, 2H); -0.05-0.04 (m, 1H); -0.21-0.13 (m, 1H). MS (ESI, *m/z*): 386 [M+H]<sup>+</sup>, 771 [2M+H]<sup>+</sup>.

### 2-(4-Bromo-3-methylphenyl)-3-[1-(3-fluorobenzyl)-1H-tetrazol-5-yl]-8-oxa-2-azaspiro[4.5]decan-1-one 16b



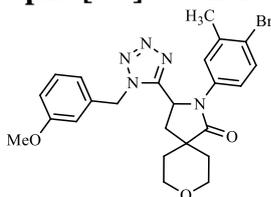
Yield – 64%, beige solid, mp >200 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 7.39 (d, 1H, *J* 8.8 Hz); 7.17-7.21 (m, 1H); 7.00-7.11 (m, 4H); 6.78-6.85 (m, 1H); 5.51 (t, 1H, *J* 7.6 Hz); 5.47 (d, 1H, *J* 15.6 Hz); 5.25 (d, 1H, *J* 15.6 Hz); 3.96-4.06 (m, 2H); 3.47-3.58 (m, 1H); 3.35-3.45 (m, 1H); 2.50 (dd, 1H, *J* 12.8, 8.0 Hz); 2.30 (s, 3H); 2.13-2.24 (m, 1H); 2.97-2.07 (m, 1H); 1.85 (dd, 1H, *J* 13.2, 7.2 Hz); 1.42-1.53 (m, 2H). MS (ESI, *m/z*): 501 [M+H]<sup>+</sup>, 1001 [2M+H]<sup>+</sup>.

**3-[1-(3-Fluorobenzyl)-1H-tetrazol-5-yl]-2-[2-(1H-imidazol-4-yl)ethyl]-8-oxa-2-azaspiro[4.5]decan-1-one 16c**



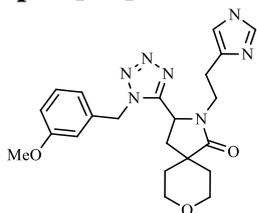
Yield – 63%, yellowish solid, mp 107-108°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 7.72 (s, 1H); 7.40 (dd, 2H, *J* 8.4, 5.2 Hz); 7.25 (t, 2H, *J* 8.8 Hz); 6.81 (s, 1H); 5.79 (d, 1H, *J* 15.6 Hz); 5.69 (d, 1H, *J* 15.6 Hz); 5.26 (dd, 2H, *J* 8.4, 5.2 Hz); 3.63-3.83 (m, 3H); 3.21-3.33 (m, 1H); 3.12-3.22 (m, 1H); 2.79-2.93 (m, 1H); 2.53-2.63 (m, 1H); 2.38- 2.47 (m, 1H); 3.08 (dd, 2H, *J* 14.4, 7.2 Hz); 1.69-1.82 (m, 2H); 1.57-1.69 (m, 1H); 1.21-1.34 (m, 2H). MS (ESI, *m/z*): 427 [M+H]<sup>+</sup>, 893 [2M+H]<sup>+</sup>.

**2-(4-Bromo-3-methylphenyl)-3-[1-(3-methoxybenzyl)-1H-tetrazol-5-yl]-8-oxa-2-azaspiro[4.5]decan-1-one 16d**



Yield – 59%, beige solid, mp 155-156°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 7.38-7.43 (m, 1H); 7.36 (d, 1H, *J* 8.4 Hz); 7.20 (d, 1H, *J* 2.4 Hz); 6.93-6.98 (m, 3H); 6.77 (dd, 2H, *J* 8.8, 2.4 Hz); 5.55 (dd, 2H, *J* 8.4, 6.8 Hz); 5.44 (dd, 2H, *J* 18.4, 16.0 Hz); 3.97-4.05 (m, 1H); 3.88 (s, 3H); 3.47-3.56 (m, 1H); 3.36-3.44 (m, 1H); 2.43 (dd, 2H, *J* 13.2, 8.0 Hz); 2.29 (s, 3H); 2.14-2.24 (m, 1H); 1.93-2.09 (m, 2H); 1.42-1.58 (m, 2H). MS (ESI, *m/z*): 427 [M+H]<sup>+</sup>, 893 [2M+H]<sup>+</sup>.

**2-[2-(1H-Imidazol-4-yl)ethyl]-3-[1-(3-methoxybenzyl)-1H-tetrazol-5-yl]-8-oxa-2-azaspiro[4.5]decan-1-one 16e**



Yield – 62%, beige solid, mp 126-127°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 7.74 (s, 1H); 7.36-7.44 (m, 1H); 7.17-7.22 (m, 1H); 6.93-7.04 (m, 2H); 6.83 (s, 1H); 5.65 (dd, 2H, *J* 20.4, 15.2 Hz); 5.11 (dd, 2H, *J* 8.4, 6.0 Hz); 3.86-3.96 (m, 4H); 3.85 (s, 3H); 3.21-3.38 (m, 2H); 3.04-3.16 (m, 1H); 2.61-2.82 (m, 2H); 1.96-2.12 (m, 2H); 1.67-1.84 (m, 2H); 1.36-1.48 (m, 1H); 1.10-1.21 (m, 1H). MS (ESI, *m/z*): 439 [M+H]<sup>+</sup>, 877 [2M+H]<sup>+</sup>.